

REMARKS

Claims 30, 31, 34, 38-46, 48, 49, 53-61, and 63-66 are pending in the application.

Claims 30, 31, 46, 63, and 64 have been amended herein. Support for the amendments to claims 30 and 31 can be found at least at paragraphs [0033] and [0042] of the specification as originally filed. Claim 46 is amended to correct an inadvertent typographical error. Claim 64 is amended to clarify dependency. Claims 67-79 are new. Support for the new claims can be found at least at paragraphs [0033], [0034], and [0035], in Examples 1 to 3, in Figure 5, and in claim 32, as originally filed.

Rejection of claim 64

Claim 64 is rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants submit the above amendment renders the rejection moot.

Withdrawal of the rejection is, therefore, respectfully requested.

Rejection of claims 30, 34, 38, 45, 46, 48, 49, 64, and 65

Claims 30, 34, 38, 45, 46, 48, 49, 64, and 65 have been rejected under 35 U.S.C. § 103(a) as being obvious over Weiss et al. (US Patent 6,143,293) in combination with Kale (US Patent Application Publication No. 2002/0127711). This rejection is respectfully traversed.

The Examiner relies on Weiss et al. as teaching a polymer scaffold comprising two or more assembled polymer membranes, wherein each membrane has a surface with varying topology including at least one feature with at least one dimension of about 25-250 microns. The Examiner states that Weiss et al. teaches that the scaffold is made of a polymer material, but does not teach that the polymer material is a hydrogel or a biopolymer hydrogel. The Examiner

relies on Kale as teaching a polymer scaffold made of a synthetic polymer (e.g., a biopolymer) of a hydrogel polymer. The Examiner states that “it would have been obvious at the time the invention was made to use a synthetic polymer (or biopolymer) of a hydrogel as a scaffold material in the scaffold of Weiss et al in view of Kale et al in order to provide a scaffold for use in the repair or replacement of tissue.”

As amended, the pending claims are directed to layered polymer scaffolds comprising a plurality of synthetic biopolymer membranes of from 1 micron to 1 millimeter in thickness which comprise at least one organized feature having at least one dimension of about 10 to 100 microns, wherein said scaffold is microfabricated by a process comprising: generating an elastomer mold; directing a synthetic biopolymer into the mold; curing the synthetic biopolymer in the mold to form a polymer membrane, wherein said membrane comprises a surface with varying topology including at least one feature with at least one dimension of about 10 to 100 microns, wherein the at least one feature is formed from the synthetic biopolymer by the process; removing the cured polymer membrane from the mold; and assembling two or more cured polymer membranes to provide a layered polymer scaffold. The claims are also directed to microfabricated polymer scaffolds comprising at least one membrane, wherein said at least one membrane i) comprises a synthetic biopolymer, ii) is from 1 micron to 1 millimeter in thickness and iii) comprises a surface with varying topology including at least one organized feature formed during from the biopolymer during microfabrication with at least one dimension of about 10 to 100 microns.

To establish a *prima facie* case of obviousness, it is necessary for the Examiner to apply a flexible teaching, suggestion, or motivation test to combine known elements in order to show that the combination is obvious. *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007).

Importantly, the *KSR* Court noted that “rejections on obviousness grounds cannot be sustained

by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” (*In re Kahn*, 441 F.3d 911,988 (CA Fed. 2006) cited with approval in KSR).

The Examiner has failed to provide a reason which would have led one of ordinary skill in the art to modify the prior art to arrive at the claimed invention. Similarly, the Examiner has failed to provide a reason why one of ordinary skill in the art would modify the Weiss et al. and Kale et al. disclosures to arrive at the claimed invention.

The Weiss et al. patent discloses methods of making “heterogeneous scaffolds” which are built by mechanical assembly of individual layer or volume elements (column 6, lines 17-19). These individual elements can be prefabricated using existing scaffold manufacturing processes such as solvent casting, shaping sections with machining, 3D printing, or molded collagen/cell constructs.

These sections can then be mechanically mated using biodegradable or non-biodegradable barbs, pins, screws, clams, staples, wires, string, or sutures. The Weiss et al. patent further discloses that “[a]ll of the aforementioned assembly strategies can be automated within a CAD/CAM environment, and all assembly can be done within liquid culture media if required.” The CAD/CAM environment refers to computer aided methodologies that allow the design of scaffolds on a relatively large scale. The scaffolds disclosed by Weiss et al. comprise membranes with a minimum of 1mm thickness and are mechanically fastened.

It is noted that the smaller dimensions of 25µm to 250µm in Weiss that are referenced by the Examiner refer to the scale of the height of the barbs that can be used to mechanically fasten membranes together (see column 8, line 47). These barbs are mechanical fasteners that are not formed from the synthetic biopolymer by the process. Rather, they are described as barbs having single or double hooks that are used to attach various layers of the scaffold to one

another. The barbs described in Weiss are not, therefore a feature formed from the synthetic biopolymer by the process with at least one dimension of about 10 to 100 μm .

Moreover, the only polymeric scaffold disclosed in the Weiss et al. patent comprises layers of hydroxyapatite, which is a rigid or semi rigid material (column 9, lines 12-13). The Weiss et al. patent fails to disclose scaffolds comprising membranes having a surface with varying topology including at least one feature formed from the synthetic biopolymer by the process with at least one dimension of about 10 to 100 μm as required by the pending claims.

There is nothing in the Kale reference that overcomes these defects in Weiss.

The Examiner's rejection appears to be grounded, at least in part, on guidelines set forth in MPEP § 2144.06, which states that "it is *prima facie* obvious to combine two or more compositions each of which is taught by the prior art to be useful for the same purpose in order to form a third composition used for the same purpose ...". However, for this conclusion to be valid, the idea of combining the compositions must flow logically from their having been individually taught in the prior art". *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be *prima facie* obvious). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron); and *Ex parte Quadranti*, 25 USPQ2d 1071 (BAPI 1992) (mixture of two known herbicides held *prima facie* obvious).

In the case of the Weiss et al. and Kale et al. references, there is no motivation present in the references to arrive at the presently-claimed invention. Weiss et al. makes large scale heterogeneous (not uniform) scaffolds which are built by mechanical assembly of individual

layer or volume elements in order to facilitate 3-dimensional tissue culture and vascularization (column 5, lines 58-62). Kale also discusses scaffolds for bone regeneration, but does not contemplate the presently-recited scaffolds having at least one organized feature formed during the microfabrication process and having at least one dimension of about 10 to 100 μm .

The instantly-claimed scaffolds are produced on a much smaller scale than those disclosed in Weiss et al. or Kale et al. Using the methods developed in the instant application, microfabricated polymer scaffolds comprising at least one membrane, which comprises a synthetic biopolymer, are from 1 micron to 1 millimeter in thickness and comprise a surface with varying topology including at least one organized feature formed by the synthetic biopolymer during the microfabrication process with at least one dimension of about 10 to 100 microns can be readily manufactured. Such scaffolds are not taught or suggested in the art.

Furthermore, absent the micromolding, microfluidic, and spin methodology disclosed in the instant application, there was no reasonable expectation of success that the claimed scaffolds could be made and the prior art methods did not allow for manufacture of scaffolds with the claimed properties. In view of the above amendments and arguments, Applicants respectfully request withdrawal of the instant rejection under 35 U.S.C. §103.

Rejection of claims 31, 53, 60, 63, and 66

The Examiner rejected claims 31, 53, 60, 63, and 66 under 35 U.S.C. § 103(a) as being unpatentable over Weiss in combination with Kale. Applicants respectfully traverse the rejection.

As discussed above, there is nothing in Weiss or Kale that would lead one having ordinary skill in the art to produce a layered polymer scaffold having at least one feature formed by the synthetic biopolymer during microfabrication that includes at least one dimension of

about 10 to 100 μm . Absent such guidance, the references cannot be said to render the claim obvious. Withdrawal of the rejection is, therefore, respectfully requested.

Rejection of Claim 61

The Examiner rejected Claim 61 under 35 U.S.C. § 103(a) as being unpatentable over Weiss in combination with Kale and further in view of Masini. Applicants respectfully traverse the rejection.

As discussed above, there is nothing in Weiss or Kale that would lead one having ordinary skill in the art to produce a layered polymer scaffold having at least one feature formed by the synthetic biopolymer during microfabrication that includes at least one dimension of about 10 to 100 μm . Applicants further submit there is nothing in Masini that would overcome this deficiency. Absent such guidance, the references cannot be said to render the claim obvious. Withdrawal of the rejection is, therefore, respectfully requested.

CONCLUSION

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 12-0080, under Order No. MITY-001CNRCE.

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

Dated: March 17, 2011

Respectfully submitted,

Electronic signature: /Debra J. Milasincic, Esq./
Debra J. Milasincic, Esq.
Registration No.: 46,931
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109-2127
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant